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Chapter 2

Long-term results of mandibular implants installed in oral cancer patients during ablative tumour surgery

This chapter is an edited version of:

Anke Korfage, Pieter J. Schoen, Gerry M. Raghoobar, Jelte Bouma, Fred R. Burlage, Jan L.N. Roodenburg, Arjan Vissink, Harry Reintsema. A 5-year follow-up of oral functioning and quality of life in oral cancer patients with implant-retained mandibular overdentures. *Head and Neck* 2011; 33(6): 831-839

Chapter 2.1

A 5-year follow-up of oral functioning and quality of life in oral cancer patients with implant-retained mandibular overdentures

Abstract

Background

This prospective study assessed the quality of life (QoL) and oral functioning of oral cancer patients up to 5 years after prosthodontic rehabilitation with mandibular implant-retained overdentures.

Methods

Fifty patients who had received implants during ablative surgery were evaluated by standardized questionnaires before and after oncological and prosthetic treatment.

Results

In 20 of the 24 surviving patients, the dentures were in function after 5 years. In these survivors, oral function remained unchanged during this period. In the 6 patients with concurrent comorbidity, global health and QoL had deteriorated, while in the patients without comorbidity global health and QoL were very high. Five-year survivors had a higher global health and better oral functioning at the 1-year evaluation than non-survivors.

Conclusion

Oral function and denture satisfaction were high and did not change over time for survivors. Deterioration in overall global health and QoL was associated with concurrent comorbidity.

Introduction

Prosthodontic rehabilitation in oral cancer patients is challenging as oral functioning is hampered due to the surgical treatment and the subsequent radiotherapy. As a consequence of this combined treatment, wearing a mandibular prosthesis is severely impeded due to the changed anatomical conditions and the intolerance of the denture-bearing mucosa to mechanical loading.¹⁻⁴ A solution for this problem might be to provide the patients an implant-retained mandibular overdenture. Implant survival in irradiated mandibles, although in general lower than in healthy patients, has been shown to be still relatively high in most articles shown in the literature, and patients have reported an improved level of oral functioning when being provided with such a denture.⁵⁻¹³ Also, assessment of the effect of such a treatment on patients' functioning and overall quality of life (QoL) is of the utmost importance.¹⁴⁻²⁰

In healthy subjects, no clinically relevant changes in oral functioning and patient satisfaction are to be expected after the first year of prosthodontic rehabilitation with an implant-retained overdenture.²¹⁻²² In oral cancer patients, it is questionable whether this is also applicable, or whether the remaining side effects of the oncological treatment and the impact of having had cancer are more prominent and veil the beneficial effect of an adequate prosthodontic rehabilitation on oral function and QoL. Thus, the purpose of this prospective study was to assess oral functioning and QoL in patients with oral cancer in whom implants had been installed during ablative tumour surgery, up to 5 years after prosthodontic rehabilitation with implant-retained mandibular overdentures.

Materials and methods

Patients and treatment

All consecutive edentulous patients with oral cancer referred to the Head and Neck Oncology group of the University Medical Center Groningen between May 1998 and April 2002 were screened to be included in this study. Inclusion criteria were edentulous upper and lower jaw, history of prosthetic problems related to lack of stability and retention of the lower denture or expected denture-related problems after oncology treatment, first malignancy in head and neck region (squamous cell carcinoma of tongue, floor of the mouth, mandibular gingiva, buccal mucosa, or oropharynx) and the need for primary ablative surgery. The patients were screened by an experienced maxillofacial surgeon (G.M.R.) and prosthodontist (H.R.). It was required that little or no improvement was to be expected from making new dentures after oncological treatment. Patients were offered conventional or implant-based treatment. Fifty-three patients fulfilled the inclusion criteria and 50 patients accepted the option of implant installation during ablative surgery. Two patients refused to have implants installed and 1 patient had never worn a prosthesis. Informed consent was provided from all patients before treatment.

Tumour surgery and implant insertion were performed at the University Medical Center Groningen. All implants (3.75 mm Brånemark screw implants with a machined surface, Nobelbiocare, Gothenburg, Sweden) were inserted during the ablative tumour surgery procedure. All implants were placed in the interforaminal region of the native bone of the mandible in a 2-stage surgical procedure. A 3-month osseointegration period before abutment connection was considered in patients not having radiotherapy after tumour surgery (18 patients). If postoperative radiotherapy was scheduled (32 patients), in general, starting within 6 weeks after surgery, the osseointegration time before abutment connection was increased to 9 months after surgery. All patients were treated by 1 maxillofacial surgeon (G.M.R.) and 1 prosthodontist (H.R.). Details are described in the article by Schoen et al.¹⁰

Functional assessments and QoL

Preoperatively, on the day of hospital admission (T_0), patients were asked to complete questionnaires regarding oral functioning and QoL. The questionnaires were administered by an investigator not involved in treatment of the patients (P.S.). Similar questionnaires and questionnaires regarding denture satisfaction and the impact of denture-related problems on social activities had to be completed 6 weeks (T_1), 1 year (T_2) and 5 years (T_3) after placing the new dentures.

QoL was assessed using the core questionnaire (Quality of Life Questionnaire-Core 30-questions [QLQ-C30]) and head and neck module (Quality of Life Questionnaire-Core 30 Head and Neck 35-questions [QLQ-H&N35]) of the European Organization for Research and Treatment of Cancer (EORTC).²³ Psychological, physical and social impact of oral disorders was assessed using the Oral Health Impact Profile (OHIP).²⁴ General QoL was assessed with the Linear Analogue Self Assessment method (LASA, 1-item version).²⁵ Denture satisfaction was assessed using a validated questionnaire consisting of 8 separate items focusing on the function of upper and lower dentures, and on specific features such as aesthetics, retention and functional comfort.²⁶ Overall denture satisfaction was expressed on a 10-point rating scale (0–10); ‘0’ being completely dissatisfied, ‘10’ being completely satisfied. Subjective chewing ability was assessed using a 9-item questionnaire on which the patient could rate on a 3-point scale their ability to chew different kinds of food.²⁷ Impact of denture problems on social activities, such as going out, and contacting and visiting people, was assessed with the Groningen Activity Restriction Scale Dentistry.²⁸

Data analysis

The obtained data were evaluated using SPSS (version 16.0 for Windows, SPSS Inc., Chicago, IL, USA). Data are shown as means \pm standard deviation (SD). Changes were stated as significant if $p < 0.05$. When comparing different groups of patients at the same time, the Mann-Whitney test was used. When comparing results within groups at different times, the Wilcoxon signed-rank test was applied.

Table 1. Patient characteristics

Age at diagnosis (years)	Sex	Primary tumour	Stage	Total intraforaminal dose (Gy)	Status
57	F	Mandibular gingiva	T4N1	–	1 (NTR)
59	M	Floor of mouth	T4N2b	–	1 (NTR)
77	F	Tongue	T3N2b	64	1 (TR)
79	M	Floor of mouth	T4N0	60	1 (TR)
52	F	Tongue/floor of mouth	T2N1	64	1 (TR)
53	M	Floor of mouth	T4N0	65	1 (TR)
69	M	Oropharynx	T2N2b	64	1 (TR)
81	M	Oropharynx	T3N1	30	2 (NTR)
52	F	Tongue	T2N1	58	2 (NTR)
61	M	Mandibular gingiva	T2N0	64	2 (TR)
81	F	Tongue/floor of mouth	T2N0	–	2 (TR)
50	M	Mandibular gingiva	T4N2b	61	2 (TR)
75	M	Tonsil	T2N0	–	3 (NTR)
64	M	Floor of mouth	T2N2c	59	3 (NTR)
59	M	Tonsil	T3N0	60	3 (NTR)
68	F	Floor of mouth	T2N0	–	3 (NTR)
65	M	Mandibular gingiva	T2N0	–	3 (NTR)
49	F	Base of tongue	T3N1	58	3 (NTR)
66	M	Mandibular gingiva	T4N2b	67	3 (NTR)
48	M	Floor of mouth	T4N1	55	3 (NTR)
78	F	Mandibular gingiva	T1N0	–	3 (NTR)
54	M	Mandibular gingiva	T4N1	62	3 (NTR)
70	M	Mandibular gingiva	T4N2b	50	3,4 (NTR)
50	M	Floor of mouth	T2N1	65	3 (TR)
66	M	Mandibular gingiva	T4N2b	64	3 (TR)
59	M	Oropharynx	T4N2b	61	3 (TR)
49	F	Floor of mouth	T2N0	57	4
76	F	Mandibular gingiva	T4N0	64	4
49	M	Floor of mouth	T2N0	50	4 (after 1 y)
71	M	Tonsil	T3N1	67	4 (after 1 y)
43	M	Tongue/floor of mouth	T2N0	–	5
65	M	Floor of mouth	T2N1	70	5
43	F	Tongue	T1N0	–	5
55	F	Tongue	T2N0	–	5
77	M	Tongue	T1N0	–	5
56	F	Floor of mouth	T1N0	–	5
41	M	Base of tongue	T3N0	63	
54	M	Tongue	T2N1	46	
51	F	Floor of mouth	T1N0	61	
64	M	Mandibular gingiva	T4N0	62	
52	M	Oropharynx	T3N0	12	
65	M	Floor of mouth	T2N0	–	
63	F	Tongue	T3N2c	62	
46	M	Tongue	T3N0	64	
54	M	Mandibular gingiva	T1N0	–	

69	M	Tongue	T2N0	–
71	M	Tongue	T2N0	–
72	M	Tongue	T2N0	–
66	M	Tongue	T3N2b	66
80	M	Tongue	T2N0	–

Abbreviations: F, female; M, male; NTR, not tumour-related; TR, tumour-related.

Notes: Patient characteristics regarding age, sex, primary tumour, staging, total interforaminal dose of radiotherapy, and status: 1: died in first year, before prosthesis could be made; 2: died in the first year after delivery of prosthesis; 3: died after first year, but before 5-year evaluation; 4: wears no prosthesis; 5: comorbidity notified at T3

Results

Patients and implants

Patient characteristics are presented in Table 1.

In total 50 patients, 35 men and 15 women (mean age 61.5 ± 11.2 years; range 41–81 years) were included at T_0 . In total, 195 implants were placed in the initial group of 50 patients; of them, 18 patients were treated by surgery only (72 implants) and 32 patients were treated with radiotherapy in addition (123 implants). During the 5-year follow-up, a total of 14 implants was lost; 13 implants in 6 patients that received radiotherapy (implant survival rate 89.4%) and 1 implant in a non-irradiated patient (implant survival rate 98.6%).

At T_2 , 1 year after denture placement, 35 overdentures were in function. Twelve patients had died (48 implants), 7 before abutment connection. Two patients had refused abutment connection (6 implants), because they did not want any additional, nontumour-related, surgery; and 1 patient had already lost three implants before abutment connection. The results of T_2 have been published previously.¹⁰ At T_3 , 5 years after denture placement, 26 patients were deceased. Another 4 patients who survived T_3 had to be excluded from follow-up, due to removal of the superstructures related to local irritation ($n=2$), loss of 3 implants ($n=1$), and the impossibility of making a denture after ablation because of derived anatomical limitations ($n=1$). Of the remaining 20 patients with functional dentures at T_3 , 9 patients were irradiated (45%).

QoL and functional assessments

EORTC QLQ-C30 and QLQ-H&N35

The results of the EORTC QLQ-C30 and QLQ-H&N35 questionnaires are presented in Table 2. The results of the evaluations after 1 and 5 years are presented for patients that survived T_3 ($n=20$), divided into irradiated (RTX, $n=9$) and non-irradiated patients (non-RTX, $n=11$). Hardly any differences between and within the groups were found. In the total group, the reported global health and general health after 5 years was lower than after 1 year ($p<0.05$) and general QoL tended to decrease ($p=0.070$). Weight loss had increased in 4 years. In irradiated patients, the mouth opening was reported more restricted and dry mouth was more severe (only significant after 1 year; $p<0.05$).

Table 2. EORTC QLQ-C30 and EORTC QLQ-H&N 35 questionnaires

EORTC QLQ-C30	After 1 year		After 5 years	
	RTX n=9	non-RTX n=11	RTX n=9	non-RTX n=11
Global health status/ quality of life	93.5 ± 8.1	74.2 ± 24.6 *	83.3 ± 12.5	64.4 ± 30.5 †
Physical functioning	85.9 ± 17.5	73.3 ± 23.5	88.9 ± 10.0	68.5 ± 33.3
Role functioning	90.7 ± 14.7	77.3 ± 31.0	88.9 ± 18.6	72.7 ± 38.2
Emotional functioning	94.4 ± 16.7	87.9 ± 22.5	91.7 ± 15.0	79.5 ± 28.0
Cognitive functioning	90.7 ± 12.1	86.4 ± 19.5	88.9 ± 8.3	75.8 ± 27.2
Social functioning	94.4 ± 11.8	86.4 ± 30.6	88.9 ± 16.7	83.3 ± 25.8
Fatigue	13.6 ± 16.5	20.2 ± 30.2	12.3 ± 14.1	24.2 ± 26.7
Nausea and vomiting	0.0 ± 0.0	3.0 ± 6.7	5.6 ± 16.7	1.5 ± 5.0
Pain	13.0 ± 16.2	10.6 ± 25.0	13.0 ± 23.2	9.1 ± 15.6
Dyspnoea	0.0 ± 0.0	24.2 ± 36.8	11.1 ± 23.6	27.3 ± 46.7
Insomnia	3.7 ± 11.1	9.1 ± 15.6	3.7 ± 11.1	9.1 ± 15.6
Appetite loss	0.0 ± 0.0	9.1 ± 30.2	7.4 ± 14.7	16.7 ± 28.3
Constipation	3.7 ± 11.1	0.0 ± 0.0	3.7 ± 11.1	3.0 ± 10.1
Diarrhoea	0.0 ± 0.0	6.1 ± 13.5	11.1 ± 23.6	6.1 ± 13.5
Financial difficulties	14.8 ± 17.6	6.1 ± 20.1	22.2 ± 37.3	10.0 ± 16.1
EORTC QLQ-H&N35				
Pain	15.7 ± 22.6	6.1 ± 9.9	19.4 ± 11.8	9.1 ± 17.3
Swallowing	19.4 ± 15.6	6.8 ± 9.0 *	12.7 ± 14.2	15.8 ± 23.4
Sensory problems	18.5 ± 17.6	15.2 ± 32.0	13.0 ± 23.2	22.7 ± 31.0
Speech problems	13.6 ± 18.2	9.1 ± 14.8	18.5 ± 22.9	14.1 ± 21.1
Trouble with social eating	22.2 ± 19.5	12.1 ± 25.6	21.3 ± 28.0	20.0 ± 28.7
Trouble with social contact	4.4 ± 11.1	5.5 ± 12.9	5.2 ± 15.6	4.2 ± 8.0
Less sexuality	16.7 ± 28.9	14.8 ± 32.7	18.8 ± 30.1	25.0 ± 34.5
Teeth	14.8 ± 33.8	9.1 ± 15.6	25.9 ± 32.4	6.7 ± 21.1
Opening mouth	44.4 ± 28.9	9.1 ± 21.6 ‡	25.9 ± 32.4	6.7 ± 14.1
Dry mouth	55.6 ± 28.9	21.2 ± 22.5 *	51.9 ± 29.4	26.7 ± 34.4
Sticky saliva	33.3 ± 28.9	12.1 ± 16.8	37.0 ± 35.1	30.3 ± 34.8
Coughing	14.8 ± 17.6	27.3 ± 25.0	14.8 ± 17.6	15.2 ± 22.9
Felt ill	3.7 ± 11.1	6.1 ± 20.1	14.8 ± 33.8	15.2 ± 22.9
Pain killers	22.2 ± 44.1	45.5 ± 52.2	22.2 ± 44.1	18.2 ± 40.5
Nutritional supplements	22.2 ± 44.1	9.1 ± 30.2	22.2 ± 44.1	18.2 ± 40.5
Feeding tube	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	18.2 ± 40.5
Weight loss	0.0 ± 0.0	9.1 ± 30.2	22.2 ± 44.1	36.4 ± 50.5
Weight gain	11.1 ± 33.3	27.3 ± 46.7	0.0 ± 0.0	9.1 ± 30.2

Abbreviations: EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30-questions; EORTC QLQ-H&N-35, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Head and Neck 35-questions.

* Significant difference between irradiated and non-irradiated patients at the same point in time $p < 0.05$.

† Significant difference between five years after placement and one year after placement $p < 0.05$.

‡ Significant difference between irradiated and non-irradiated patients at the same point in time $p < 0.01$.

Notes: Results of the functional scales, symptom scales and single items of the EORTC QLQ-C30 and multi-item scales and single items of the EORTC QLQ-H&N 35 questionnaires for the 5 years surviving patients with a functional implant-retained overdenture, at 1 year and 5 years after placement of the dentures (for irradiated (RTX) and non irradiated patients (*non-RTX*) patients). For the 1-year results (n=35 patients) see Schoen et al.¹⁰

Table 3. Comorbidity versus no comorbidity

EORTC QLQ-C30	Comorbidity n=6	No comorbidity n=14
Global health status/ quality of life	48.6 ± 27.6	83.3 ± 16.3 *
Physical functioning	50.0 ± 35.5	89.5 ± 9.3 *
Role functioning	55.6 ± 44.3	90.5 ± 16.9
Emotional functioning	69.4 ± 33.6	91.7 ± 14.2
Cognitive functioning	63.9 ± 30.6	89.3 ± 10.5
Social functioning	69.4 ± 28.7	92.9 ± 14.2
Fatigue	40.7 ± 26.0	9.5 ± 12.2 *
Nausea and vomiting	2.8 ± 6.8	3.6 ± 13.4
Pain	16.7 ± 18.3	8.3 ± 19.3
Dyspnoea	61.1 ± 49.1	2.4 ± 8.9 †
Insomnia	11.1 ± 17.2	4.8 ± 12.1
Appetite loss	33.3 ± 33.3	4.8 ± 12.1
Constipation	5.6 ± 13.6	2.4 ± 8.9
Diarrhoea	11.1 ± 17.2	7.1 ± 19.3
Financial difficulties	16.7 ± 18.3	15.4 ± 32.2

Abbreviations: EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30-questions

* Significant difference between patients with and without comorbidity after five years $p < 0.01$.

† Significant difference between patients with and without comorbidity after five years $p < 0.05$.

Notes: Results of the functional scales, symptom scales and single items of the EORTC QLQ-C30 for patients with and without comorbidity, 5 years after placement of the dentures.

Comorbidity

Based on the data in the patients' medical histories, patients were subdivided into 2 groups based on the comorbidity noticed at T_3 (Table 3). Six patients were identified with comorbidity, including secondary radiotherapy (after T_2) in the head and neck region ($n=2$), an established stroke, lung metastases, severe lung emphysema and a transient ischemic attack (Table 1). When looking into detail in these patients, global health, physical function, fatigue and dyspnoea were significantly worse in these patients with comorbidity. QoL and global health were very high in patients without comorbidity and remained at the same level between T_2 and T_3 . When comparing the T_1 -data and T_2 -data, there was a progressive decrease in general health, global health, and cognitive function over time in patients with comorbidity. A tendency towards a decrease in cognitive function ($p=0.078$) and an increase in weight loss ($p=0.083$) with time was also seen in patients with comorbidity.

Radiotherapy

The global health status in irradiated patients was higher than non-irradiated patients. However, 5 patients with comorbidity were among the 11 non-irradiated patients, whereas there was only 1 patient with comorbidity among the 9 irradiated patients. When excluding

Table 4. OHIP questionnaire

	After 1 year		After 5 years	
	RTX n=9	non-RTX n=11	RTX n=9	non-RTX n=11
OHIP14	12.4 ± 10.9	6.3 ± 8.9 *	12.8 ± 12.1	6.7 ± 6.5
Functional limitation	12.0 ± 6.5	6.6 ± 5.4 †	11.1 ± 5.9	7.3 ± 4.8
Physical pain	7.0 ± 9.5	4.0 ± 6.3	11.0 ± 9.6	4.3 ± 6.1 ‡
Physical disability	13.0 ± 10.7	5.9 ± 8.1 §	10.4 ± 10.5	6.2 ± 6.3
Psychological discomfort	2.1 ± 5.3	0.8 ± 1.9	3.4 ± 5.8	1.0 ± 2.0
Psychological disability	2.0 ± 4.3	0.9 ± 2.4	1.9 ± 3.6	0.9 ± 1.0
Social disability	1.3 ± 2.5	0.8 ± 1.8	1.3 ± 2.7	0.9 ± 1.3

Abbreviations: OHIP, Oral Health Impact Profile

* Significant difference between irradiated and not irradiated patients at the same point in time; $p < 0.05$.

† Tendency towards difference between irradiated and non-irradiated patients at the same point in time; $p = 0.056$.

‡ Tendency towards difference between irradiated and non-irradiated patients at the same point in time; $p = 0.067$.

§ Tendency towards difference between irradiated and not irradiated patients at the same point in time; $p = 0.056$.

Notes: Results of the Oral Health Impact Profile (OHIP) questionnaire, at 1 year and 5 years after placement of the dentures, for irradiated (RTX) and non-irradiated (non-RTX) 5-years survivors with a functional implant-retained overdenture. For the 1-year results ($n=35$ patients) see Schoen et al¹⁰.

the patients with comorbidity, the differences in the EORTC QLQ-C30 disappeared.

At T_2 , the irradiated patients reported a dryer mouth, less opening of the mouth and more difficulties with swallowing in the QLC-H&N35 questionnaires (Table 2). At T_3 , the differences between irradiated and non-irradiated patients did not reach significance, although trends were seen towards a dryer mouth ($p=0.095$) and more pain ($p=0.056$) in irradiated patients. When taking comorbidity into account, we saw several differences in the QLC-H&N35; the irradiated patients reported a dryer mouth, more pain ($p<0.05$), less opening of the mouth, more problems in speech and more problems related to the dentures ($p=0.059$).

When comparing the irradiated patients with the non-irradiated patients, over time, global health and global health related QoL tended to decrease for the irradiated patients ($p=0.059$ and $p=0.066$).

Survivors versus non-survivors

When looking retrospectively into the 35 patients with functional dentures at T_2 , there were some differences between the 5-year survivors with functional dentures ($n=20$) and those patients that did not make it to T_3 ($n=12$); the results are not depicted in a table. At T_2 , the 5-year survivors had reported a higher global health and fewer problems with swallowing ($p<0.05$) than the nonsurvivors. Nonsurvivors tended to report more pain and a lower general QoL than the survivors ($p=0.068$).

OHIP, functional assessments, social restrictions and denture satisfaction

The OHIP results are presented in Table 4, and the results of questionnaires regarding oral functioning and denture satisfaction are presented in Table 5. Over time, there were no changes in results for the total group, neither were differences seen between patients with or without comorbidity.

Table 5. Oral functioning and denture satisfaction

	After 1 year		After 5 years	
	RTX n=9	non-RTX n=11	RTX n=9	non-RTX n=11
GARS-D	2.6 ± 4.6	1.9 ± 3.9	3.5 ± 5.0	2.8 ± 5.1
Denture satisfaction	12.9 ± 4.8	11.6 ± 4.4	13.9 ± 4.8	11.8 ± 3.1
Overall denturesatisfaction	8.4 ± 1.2	8.5 ± 1.4	8.5 ± 1.3	8.9 ± 1.1
Chewing/eating	7.4 ± 7.0	3.8 ± 4.3	6.0 ± 6.7	4.6 ± 4.9
LASA quality of life	81.8 ± 18.5	69.3 ± 24.9	87.4 ± 9.5	65.3 ± 28.7 *

Abbreviations: GARS-D, Groningen Activity Restriction Scale Dentistry; LASA, Linear Analogue Self Assessment.
* Tendency towards difference between irradiated and non-irradiated patients at the same point in time $p = 0.055$.
Notes: Results of questionnaires regarding oral functioning and denture satisfaction, at 1 year and 5 years after placement of the dentures, for irradiated (RTX) and non-irradiated (non-RTX) patients with a functional implant-retained overdenture. For the 1-year results ($n = 35$ patients) see Schoen et al.¹⁰

Radiotherapy

A tendency toward more pain was reported in the OHIP in the irradiated group ($p = 0.067$) between T_2 and T_3 . When excluding patients with comorbidity, more differences were found between irradiated patients and non-irradiated patients: at T_3 irradiated patients reported more functional limitations and physical pain ($p < 0.05$) than non-irradiated patients and a tendency was seen towards more physical disability ($p = 0.081$) and a higher score in the handicap domain ($p = 0.081$) in irradiated patients. Previously, we reported that overall denture satisfaction was higher in non-irradiated than in irradiated patients at T_2 ,¹⁰ but in the irradiated patients denture satisfaction was also rather high. On the other scales of functional assessment the non-irradiated patients showed better results than the irradiated patients at T_2 .¹⁰ At T_3 , denture satisfaction again scored high, but denture satisfaction and functional assessment showed no differences between irradiated and non-irradiated patients. Overall QoL, as measured with the LASA, showed, as did the EORTC QLQ-C30, a higher QoL for the irradiated patients after five years ($p = 0.055$), but this difference disappeared when taking comorbidity into account.

Survivors versus non-survivors

At T_1 , nonsurvivors reported to be more concerned with the future functioning of their dentures than the 5-year survivors ($p < 0.05$). There tended to be more social restrictions

and chewing problems ($p=0.095$ and $p=0.074$) for the nonsurvivors than for the survivors. At T_2 , survivors reported less social restrictions than nonsurvivors ($p=0.059$). Also, survivors tended to be more satisfied with their dentures than the nonsurvivors ($p=0.087$).

Discussion

The surviving 20 patients with functional dentures did not report a difference in oral function between 1 and 5 years after prosthetic rehabilitation. The observed deterioration in overall global health and QoL was strongly associated with concurrent comorbidity in 6 patients. For patients without known comorbidity general QoL and global health were very high.

No difference in oral function was reported at the 1 year and 5 year follow after placement of the prostheses. This observation is comparable to results of studies in healthy subjects.²¹⁻²² The oral function of the patients in this study was reasonable, but lower than in healthy subjects.²⁷ Still, the denture satisfaction was very high. However, there was a difference in global health, oral and social functioning and denture satisfaction between the 5-year survivors and the nonsurvivors, indicating a 'natural' selection of patients. This is in agreement with the findings of other studies³⁰⁻³¹, where high scores of functioning scales and low scores on symptom items at 1-year follow up seemed to predict a high survival at 5 years. In our study, survivors reported fewer problems with swallowing and less restrictions in social activities. The nonsurvivors were more concerned with the future functioning of their dentures than the survivors. An explanation can be that the 20 patients with a functional denture had a lower percentage of large tumours compared to the nonsurvivors (Table 1), thus needing less extensive surgery with less morbidity. Also, among the deceased and excluded patients at T_3 , a larger percentage had received radiotherapy in comparison to the survivors, probably giving less favourable oral conditions.

The scores of the EORTC QLC-C30 and QLC-H&N35 questionnaires at T_3 are comparable to the results of other QoL studies in patients with head and neck cancer.³⁰⁻³⁴ The patients without known comorbidity reported high scores comparable to those of healthy subjects. This observation indicates that even after oncological treatment patients still can reach 'normal' health levels. Furthermore, in previous studies, the question was raised whether patients do value oral rehabilitation as essential in their life after head and neck cancer. In one study reporting on general QoL in patients without an implant-borne overdenture, no difference in general QoL was found between patients that wore their mandibular dentures and patients that did not.³⁵ A review relating QoL to functional outcome also showed no difference in QoL between patients with a conventional dental/tissue-supported denture, an implant-retained overdenture and patients without dentures.¹⁷ Most patients reported satisfactory outcomes regardless of the type or presence of prosthetic rehabilitation. This finding is in agreement with the findings of Murphy et al¹⁸, as data correlated QoL with functional outcome and symptom burden often fails to demonstrate a consistent

relationship. The latter authors suggested that this may be attributed to methodological issues in the study design or the patient's ability to adapt to functional and symptom control problems.

It is obvious that certain stages of disease and cancer treatment will lead to disastrous anatomical or physiological conditions in which oral rehabilitation cannot be restored to a level comparable to the level before onset of the disease. However, the patients' ability to adapt to functional problems and to accept the loss of some oral functions should not be underestimated. Another conclusion could be that validated sensitive instruments to rate the influences of oral rehabilitation on QoL are still not available for general application. Regarding general health-related QoL, such validated instruments are commonly available.¹⁵ However, these general health-related QoL questionnaires seem to lack the discriminating ability to measure the effects of prosthodontic treatment on QoL in oral cancer patients. Efforts have been done to develop instruments that might solve this problem such as Liverpool Oral Rehabilitation Questionnaire (LORQ), which was developed in 2004 and has been used on since.³⁶⁻³⁹ Also more specific questionnaires that focus on head and neck function, such as speech and swallowing are currently available.⁴⁰ Unfortunately we were not able to use such questionnaires as these questionnaires were not available at the time of inclusion of our patients into our study.

It seems that other factors such as comorbidity are far more important in determining the patients' QoL being an important caution that has to be considered when interpreting the results of the questionnaires regarding general health. With a closer look, the decrease in QoL we observed appeared to be caused by a small group of patients with severe comorbidity. Most patients with comorbidity were not irradiated. When taking this comorbidity into account, the specific head and neck module reveals differences between the irradiated and non-irradiated patients even after 5 years, which can be related to the late effects of the radiotherapy, such as dry mouth, less opening of the mouth and problems with swallowing and speech. Terrell et al⁴¹ ranked comorbidity to be the second greatest predictor of decreased QoL in head and neck cancer patients. In our study, we did not apply standard comorbidity measures as the Adult Comorbidity Evaluation (ACE27), that are currently used in studies to code and quantify comorbidity⁴²⁻⁴⁴ Nevertheless, we were able to indicate that comorbidity apparently played a larger role in decreased QoL scores than radiotherapy. However, 2 patients received radiotherapy between T₂ and T₃ due to recurrent disease. In the analysis these patients were scored as non-irradiated (intention-to-treat procedure) and were considered as having comorbidity. This could also explain why differences are only found in the head and neck module when excluding patients with comorbidity.

Implant loss was higher in patients that received radiotherapy post-tumour surgery. This is in agreement with other studies.^{5,7,8,11} A review reports that the increase in the risk of implant loss in irradiated patient may be up to 12 times greater; however, the magnitude of this difference should be accepted with caution since studies making these comparisons

are of poor to moderate quality.¹² The failure rate of 10.6% in irradiated bone over a period of 5 years found in our study is considered good. However, 26 patients had died and the percentage of patients that had received postoperative radiotherapy decreased over time amongst the survivors (73% at baseline vs. 54% 5 years after placement of the dentures). This could have contributed to the relatively low failure rate of implants in irradiated bone. The percentage of patients rehabilitated with the help of dental implants placed after ablative surgery and postoperative radiotherapy varies in the literature. Reported percentage are between 22-91%,^{9,14, 45-50} depending largely on the type of patients included, the type of reconstruction, the survival rate of patients and implants and the length of the follow-up. In our study where the implants were placed during ablative surgery, a relatively large number of the living patients was rehabilitated with dentures (at T₂: 92%, at T₃: 83%). No delay or complications in oncological treatment were seen due to the placement of the implants at that time. Still, 2 patients refused abutment connection because of the expected extra burden of abutment connection surgery. Also, from previous data, it was concluded that many patients refrain from further surgery, including implant installation, after they survived head and neck oncology treatment, despite an improvement of oral functioning was to be expected postsurgery³⁵. When placing the implants during ablation, a significant time reduction of (pre)prosthetic rehabilitation can be achieved. Consequently, a large percentage of patients and even patients with a worse general prognosis can benefit for some time from the improvements in aesthetics and oral function. Future study might identify patients who are less likely to benefit from implant placement per ablation. Our study indicates that implant installation during ablative surgery results in a high percentage of rehabilitated patients, also after 5 years. From a health economics point of view, however, the loss of resources needs further consideration by performing a cost-effectiveness analysis.

Based on this study we conclude that the overall global health and QoL deteriorated in the total group between 1 and 5 years after placement of the dentures, which was due to concurrent comorbidity in a small number of patients. The global health and QoL for patients without comorbidity was very high. A large number of surviving patients could benefit from an implant-retained mandibular overdenture (83%) after 5 years. The oral function and denture satisfaction was high and did not change over time for the 5-year survivors.

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Chapter 2.2

Benefits of dental implants
installed during ablative tumour
surgery in oral cancer patients:
a prospective 5-year clinical trial

Abstract

Objective

This prospective study assessed treatment outcome and patient satisfaction of oral cancer patients with a mandibular overdenture on implants up to 5 years after treatment.

Materials and methods

At baseline, 50 consecutive edentulous oral cancer patients, in whom prosthetic problems were expected after oncological treatment, were evaluated by standardized questionnaires and clinical assessments. All implants were installed during ablative tumour surgery in native bone in the interforaminal area. About two-thirds of the patients (n=31) had radiotherapy post-surgery (dose >40 Gy in the interforaminal area).

Results

At the 5-year evaluation, 26 patients had passed away and four patients had to be excluded from the analyses, because superstructures were not present, due to persistent local irritation (n=2), loss of three implants (n=1) and the impossibility of making an overdenture related to tumour and oncological surgery-driven anatomical limitations (n=1). In the remaining 20 patients, the prosthesis was still in function (76 implants). During the 5-year follow-up, in total 14 implants were lost, 13 in irradiated bone (survival rate 89.4%, dose >40 Gy) and one in non-irradiated bone (survival rate 98.6%). Peri-implant tissues had a healthy appearance and remained healthy over time. Patients were satisfied with their dentures.

Conclusions

It was concluded that oral cancer patients can benefit from implants installed during ablative surgery, with a high survival rate of the implants, a high percentage of rehabilitated patients and a high denture satisfaction up to 5 years after treatment.

Introduction

Prosthetic rehabilitation of oral cancer patients is challenging. Often, oral functioning declines after surgical treatment and is even more impaired if combined with radiotherapy, due to the adverse biological changes resulting from exposure of the oral tissues and salivary glands to ionizing radiation (Vissink et al. 2003). In edentulous cancer patients, in addition, the possibility of making a well-functioning lower denture is often also severely impeded because of changed anatomical conditions (restricted neutral zone) and intolerance of the denture-bearing mucosa to mechanical loading (Buchbinder et al. 1989; Hayter & Cawood 1996; Marker et al. 1997; Misiek & Chang 1998). A solution for this problem can be the fabrication of an implant-retained mandibular overdenture, as implant survival in irradiated mandibles has been shown to be relatively high and patients report an improved level of oral functioning when being provided with such a denture (Granström et al. 1994; Granström 2003, 2005; Müller et al. 2004; Yorit et al. 2006; Colella et al. 2007; Schoen et al. 2007, 2008; Idhe et al. 2009). When considering patients to be treated for oral cancer, timing of implant installation is still subject of discussion. So far, no difference is found in implant loss between the installation of implants before or after radiotherapy (Colella et al. 2007); however, the far majority of studies report on implants installed after radiotherapy.

Named advantages of implant installation during ablative tumour surgery include (Schoen et al. 2004): 1. implant surgery in an area compromised by radiotherapy can be avoided, thus reducing the risk of late complications, such as development of osteoradionecrosis; 2. initial implant healing (osseointegration) will take place before irradiation; 3. the patient can benefit from the support of the implants at an earlier stage after treatment, e.g. concerning the rehabilitation of speech and swallowing; 4. there is no need for adjunctive prophylaxis such as the long-term use of antibiotics or hyperbaric oxygen therapy. Furthermore, it has been shown that many patients were unwilling to undergo another surgical intervention when installation of implants was proposed, even when an improvement in oral function was predicted (Kwakman et al. 1997; Schoen et al. 2007). Besides these benefits, the risks of installing implants during ablative surgery have to be named as well: 1. improper implant positioning, especially when ablative surgery will result in gross alterations in the anatomical situation and/or intermaxillary relationship; 2. interference with or delay of oncological therapy including radiotherapy; 3. development of post-treatment complications caused by installation of implants during ablative surgery; and 4. lack of use of implants, due to early tumour recurrence or patients refusing abutment connection surgery.

In healthy subjects, no further change in oral functioning and patients' satisfaction is to be expected after the first year of prosthetic rehabilitation with an implant-retained overdenture (Raghoobar et al. 2003; Meijer et al. 2009). In oral cancer patients, it is questionable whether this is also applicable, or the remaining side effects of the oncological treatment and the impact of having had cancer are more prominent and veil the beneficial effects of an adequate prosthetic rehabilitation on oral function.

The objective of this prospective study was to assess the treatment outcomes (condition of peri-implant tissues, implant survival, reported denture satisfaction and subjective chewing ability) of oral cancer patients with implant-retained mandibular overdentures, in whom the implants were installed during ablative tumour surgery, up to 5 years after placement of the overdenture.

Material and methods

Patients and treatment

All consecutive edentulous patients with cancer in the mandibular region referred to the Head and Neck Oncology Group of the University Medical Center Groningen between May 1998 and April 2002 were screened to be included in this study. The criteria for inclusion were an edentulous upper and lower jaw, existing prosthetic problems related to lack of stability and retention of the lower denture or to be expected denture-related problems after oncology treatment, first malignancy in the head and neck region (squamous cell carcinoma of tongue, floor of the mouth, mandibular gingiva, buccal mucosa or oropharynx) and need for primary ablative surgery (for patients' characteristics see Table 1). The patients were screened by an experienced maxillofacial surgeon (G.M.R.) and prosthodontist (H.R.). All patients were offered conventional or implant-based treatment. They accepted the option of implant installation during ablative surgery, and informed consent was obtained from all patients as requested by the human ethics committee of the University Medical Center Groningen.

Tumour surgery and implant insertion were performed at the Groningen University Medical Center. All implants (3.75 mm Brånemark screw implants with a machined surface, Nobelbiocare, Gothenburg, Sweden) were inserted immediately after ablation of the tumour. All implants were installed in the interforaminal region of the native bone of the mandible in a two-stage surgical procedure. An osseointegration period of 3 months before abutment connection was considered in patients not needing radiation therapy after tumour surgery. If postoperative radiation therapy was scheduled, starting within 6 weeks after surgery, the osseointegration time before abutment connection was increased to 9 months after surgery. In patients receiving radiotherapy, the cumulative absorbed dose at the implant locations was calculated using the computed tomography data available for the treatment planning (Wang et al. 1998).

All patients received a Dolderbar superstructure with a clip-retained mandibular overdenture and a conventional upper denture. Thus, the overdentures were mainly implant borne but also tissue borne, providing a mixed support. A bilateral balanced occlusal scheme was applied to create a steady occlusal loading of the prostheses. All patients were treated by one experienced maxillofacial surgeon (G.M.R.) and one experienced prosthodontist (H.R.). Home care instructions with regard to maintenance of the dentures and peri-implant tissues were given (for details see Schoen et al. 2008).

Clinical assessments and radiographic analysis

The clinical assessments included a survey of the dental status, the oral condition and the prosthetic rehabilitation. Postoperative complications and implant survival were recorded from the time of surgery until 5 years after placement of the dentures. Periodontal indices were assessed 6 weeks (T1), 1 year (T2) and 5 years (T3) after placing the new dentures. The periodontal indices included plaque index (Mombelli et al. 1987), bleeding index (Mombelli et al. 1987), gingival index (Loë & Silness 1963), probing depth and implant mobility (Teerlinck et al. 1991). Probing depth was measured at four sites of each implant (mesially, labially, distally and lingually) using a periodontal probe (Merit B, Hu Friedy, Chicago, IL, USA) after removal of the bar; the distance between the marginal border of the mucosa and the tip of the periodontal probe was scored as the probing depth. Mobility of the implants was determined quantitatively by perio test values after removal of the bar and (re)tightening of all the abutments. The clinical assessments at T1, T2 and T3 were performed by two investigators (P.J.S. and H.R.).

At the start of prosthetic loading (T1) and every subsequent year until T3, rotational panoramic radiographs were made to evaluate the implant-surrounding bone height. The bone loss measurements were executed by two researchers (A.K. and H.R.). Possible bone loss around the implants was classified according to the scale proposed by Geertman et al. (1996):

- 0: no apparent bone loss;
- 1: reduction of bone level not exceeding one-third of the length of the implant;
- 2: reduction of bone level exceeding one-third of the length of the implant but not exceeding one-half of the length of the implant;
- 3: reduction of bone level exceeding one-half of the length of the implant; and
- 4: total reduction of bone along the implant.

Functional assessments and denture satisfaction

Preoperatively, i.e. on the day of hospital admission (T0), patients were asked to complete questionnaires regarding oral functioning and quality of life. The questionnaires were administered by the investigator (P.J.S.) who was not involved in the oncological and prosthodontic treatment of the patients. Similar questionnaires had to be completed 6 weeks (T1), 12 months (T2) and 5 years (T3) after placing the new dentures, as well as questionnaires regarding denture satisfaction and the impact of denture-related problems on social activities. Denture satisfaction was assessed using a validated questionnaire consisting of eight separate items focusing on the function of upper and lower dentures, and on specific features such as aesthetics, retention and functional comfort (Vervoorn et al. 1988). Overall denture satisfaction was expressed on a 10-point rating scale (0–10); “0” being completely dissatisfied and “10” being completely satisfied. Subjective chewing ability was assessed using a nine-item questionnaire on which the patient could rate on a three-point scale their ability to chew different kinds of food (Stellingsma et al. 2005).

Data analysis

The data of this longitudinal prospective clinical trial were evaluated using SPSS (version 16.0 for Windows, SPSS Inc., Chicago, IL, USA). Data are shown as means \pm standard deviation (SD). Changes were stated as significant if $P < 0.05$. For the continuous data, when comparing irradiated with non-irradiated patients at the same time point, the independent t-test was used, and when comparing results within groups at different time points, the t-test for dependent samples was applied. For ordinal data, when comparing irradiated with non-irradiated patients at the same time point, the Mann–Whitney U- test was used, when comparing within groups at different time points, the Wilcoxon signed ranks test was used. Implant survival in radiated versus non-radiated patients was tested using a chi square test.

Results

Patients

In total, 50 patients (35 men and 15 women; mean age 61.5 ± 11.2 years; range 41–81 years) were included (Table 1).

At T2 12 patients and at T3 in total 26 patients had passed away (Fig. 1). Regarding the deaths, 11 were tumour related and 15 were non-tumour related. After ablative surgery, 31 of the initial 50 patients (62%) were treated with radiotherapy (dose $>40\text{Gy}$). In the group of survivors after 5 years, 13 of the remaining 24 patients (54%) had been treated with radiotherapy (dose $>40\text{ Gy}$) after surgery. Four patients did not wear their prosthesis (for reasons see below). Of the 20 patients with functional prostheses after 5 years, nine patients (45%) had been irradiated.

One year after placement, 35 overdentures were in function (12 patients had passed away; three patients had no abutment connection). Five years after placement, 20 overdentures remained in function (Fig. 1).

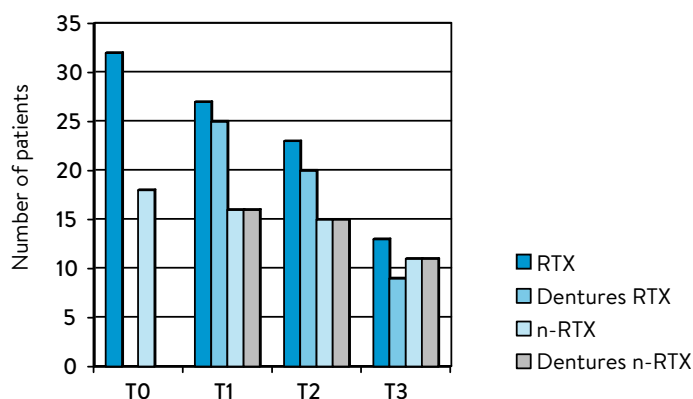
Table 1. Patients' characteristics

Patient characteristics regarding age, sex, primary tumour, staging, total interforaminal dose of radiotherapy and status: 1, died in first year, before prosthesis could be made; 2, died in the first year after delivery of prosthesis; 3, died after first year, but before 5 year evaluation; 4, wears no prosthesis (NTR: death not related to the primary tumour; TR: death related to the primary tumour).

Age at diagnosis (years)	Sex	Primary tumour	Stage	Total intraforaminal dose (Gy)	Status
57	F	Mandibular gingiva	T4N1	–	1 (NTR)
59	M	Floor of mouth	T4N2b	–	1 (NTR)
77	F	Tongue	T3N2b	64	1 (TR)
79	M	Floor of mouth	T4N0	60	1 (TR)
52	F	Tongue/floor of mouth	T2N1	64	1 (TR)
53	M	Floor of mouth	T4N0	65	1 (TR)
69	M	Oropharynx	T2N2b	64	1 (TR)
81	M	Oropharynx	T3N1	30	2 (NTR)
52	F	Tongue	T2N1	58	2 (NTR)
61	M	Mandibular gingiva	T2N0	64	2 (TR)
81	F	Tongue/floor of mouth	T2N0	–	2 (TR)
50	M	Mandibular gingiva	T4N2b	61	2 (TR)
75	M	Tonsil	T2N0	–	3 (NTR)
64	M	Floor of mouth	T2N2c	59	3 (NTR)
59	M	Tonsil	T3N0	60	3 (NTR)
68	F	Floor of mouth	T2N0	–	3 (NTR)
65	M	Mandibular gingiva	T2N0	–	3 (NTR)
49	F	Base of tongue	T3N1	58	3 (NTR)
66	M	Mandibular gingiva	T4N2b	67	3 (NTR)
48	M	Floor of mouth	T4N1	55	3 (NTR)
78	F	Mandibular gingiva	T1N0	–	3 (NTR)
54	M	Mandibular gingiva	T4N1	62	3 (NTR)
70	M	Mandibular gingiva	T4N2b	50	3,4 (NTR)
50	M	Floor of mouth	T2N1	65	3 (TR)
66	M	Mandibular gingiva	T4N2b	64	3 (TR)
59	M	Oropharynx	T4N2b	61	3 (TR)
49	F	Floor of mouth	T2N0	57	4
76	F	Mandibular gingiva	T4N0	64	4
49	M	Floor of mouth	T2N0	50	4 (after 1 y)
71	M	Tonsil	T3N1	67	4 (after 1 y)
43	M	Tongue/floor of mouth	T2N0	–	
65	M	Floor of mouth	T2N1	70	
43	F	Tongue	T1N0	–	
55	F	Tongue	T2N0	–	
77	M	Tongue	T1N0	–	
56	F	Floor of mouth	T1N0	–	
41	M	Base of tongue	T3N0	63	
54	M	Tongue	T2N1	46	
51	F	Floor of mouth	T1N0	61	
64	M	Mandibular gingiva	T4N0	62	
52	M	Oropharynx	T3N0	12	

65	M	Floor of mouth	T2N0	-
63	F	Tongue	T3N2c	62
46	M	Tongue	T3N0	64
54	M	Mandibular gingiva	T1N0	-
69	M	Tongue	T2N0	-
71	M	Tongue	T2N0	-
72	M	Tongue	T2N0	-
66	M	Tongue	T3N2b	66
80	M	Tongue	T2N0	-

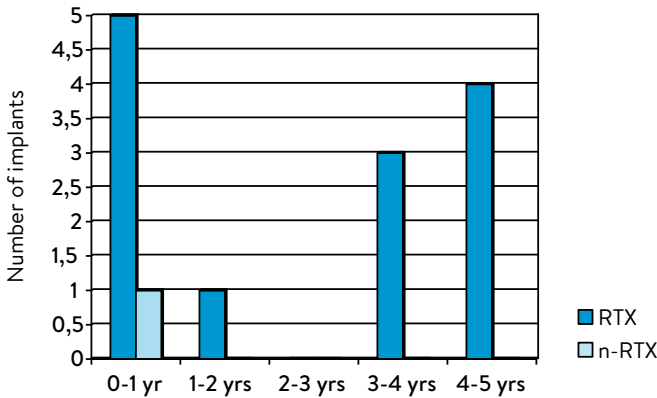
Figure 1. Number of patients alive and dentures worn at baseline (T0), after delivering the dentures (T1), after 1 year (T2) and after 5 years (T3). RTX: irradiated patients; n-RTX: non-irradiated patients



The other four surviving patients had to be excluded due to removal of the superstructures before T3 because of persistent local irritation of the soft tissue near the superstructure (n=2), the impossibility of making a denture due to anatomical limitations resulting from ablative surgery (n=1) and loss of three implants (n=1). In the latter patient, new implants were installed after bone healing and a new prosthesis was made, which was still in function after 5 years. However, this patient was excluded from the 5-year evaluation data as the new implants had been installed after surgery and radiotherapy.

In total, 195 implants were installed in the initial group of 50 patients. In one patient, three implants were installed because of lack of space in the interforaminal area to install four implants with an appropriate distance between the implants (no radiotherapy), and in two patients, two implants were installed instead of four due to anatomical limitations resulting from ablative surgery (resections of the mandible; both patients were irradiated). In total, 14 implants were lost during follow-up, mainly in irradiated patient (chi square test, $P < 0.05$); viz. 13 implants in seven patients who received radiotherapy (n=123) (implant survival rate 89.4%) and one implant in a patient treated without radiotherapy (n=72) (implant survival rate 98.6%) (Fig. 2).

Figure 2. Number of implants lost during follow-up. RTX: implants in irradiated patients; n-RTX: implants in non-irradiated patients



Six of these 14 implants were lost before the overdenture could be made. Eight implants were lost after prosthetic loading; all installed in irradiated bone.

In the 20 patients with a functional overdenture at T3, in total 79 implants (19 x 4 implants, 1 x 3 implants) were installed during ablation. In this group, three implants had been lost meanwhile (two in irradiated patients after placement of the overdenture and one in a non-irradiated patient before placement of the overdenture) giving an implant survival rate of 96.2% in this group.

Clinical and radiographic assessments

No postoperative complications or delay in oncological treatment occurred related to implant surgery. The mean scores on the indices for peri-implant parameters were low at all evaluations (Table 2). There were no clinically relevant differences in clinical peri-implant parameters between the irradiated patients and the non-irradiated patients (independent t-test, $P > 0.05$). Also over time, there were no differences in clinical parameters between the evaluation time points for the irradiated patients and the non-irradiated patients (independent t-test, $P > 0.05$). Regarding the radiographic scores, there was a significant increase between T1 and T3 for both irradiated patients and non-irradiated patients (Table 2, Wilcoxon signed ranks test, $z = -2.366$ and -2.670 , $P = 0.018$ and 0.008 , respectively).

Table 2. Mean and median scores of the peri-implant parameters at T1, T2 and T3 for the 20 patients wearing an implant-retained mandibular overdenture at T3

	T1						T2						T3					
	RTX (n = 9) *			N-RTX (n = 11) *			RTX (n = 9)			N-RTX (n = 11)			RTX (n = 9)			N-RTX (n = 11)		
	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD
Plaque index (score 0 to 3)	1	0.9	0.8	1	0.7	0.6	1	1.0	0.6	1	0.9	0.7	1	0.8	0.5	1	0.9	0.8
Calculus (score 0 to 1)	0	0.1	0.3	0	0.1	0.3	0	0.0	0.0	0	0.0	0.1	0	0.1	0.2	0	0.2	0.3
Bleeding index (score 0 to 3)	1	1.2	0.6	1	0.8	0.7	1	1.4	0.4	1	1.0	0.5	1	1.4	0.4	1	0.5	0.9
Gingiva index (score 0 to 3)	0	0.5	0.6	0	0.3	0.4	0	0.2	0.3	0	0.0	0.0	0	0.4	0.4	0	0.4	0.7
Pocket depth (mm)	n.a.	2.0	0.6	n.a.	2.4	0.4	n.a.	3.0	0.5	n.a.	2.9	0.7	n.a.	2.3	0.4	n.a.	2.1	1.8
Width of attached gingiva (score 0 to 3)	2	1.5	0.7	2	1.8	0.5	2	1.3	0.7	2	1.5	0.7	2	1.7	0.7	2	2.1	0.6
Periotest (scoring range: -8 to 50)	n.a.	-4.4	0.9	n.a.	-4.3	1.2	n.a.	-2.4	2.9	n.a.	-4.5	1.5	n.a.	-3.2	2.5	n.a.	-4.7	0.9
Radiographic analysis (scoring 0-4)	0	0.3	0.4	0	0.2	0.3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	1	1.0	0.4	1	0.9	0.7

A higher score indicates more plaque, calculus, bleeding, pocket depth, width of attached gingiva and less stability of the implant (periotest).

* RTX: irradiated patients; N-RTX: non-irradiated patients; n.a.: not applicable; n.d.: not done

Denture satisfaction and chewing ability

The denture satisfaction of the patients with a functional prosthesis is presented in Table 3, the overall denture satisfaction data are given in Table 4 and the results of the chewing ability questionnaire are shown in Table 5. The results are presented for the patients who survived T2 (n=35) and patients who survived T3 (n=20), respectively, divided into irradiated patients and non-irradiated patients, in order to depict the T1, T2 and T3 data for the same subgroup of patients (i.e. survivors).

Table 3. Denture satisfaction

Satisfaction Range (1-5)*	Survivors at T2 (n=35)					
	T1			T2		
	total	RTX	n-RTX	total	RTX	n-RTX
	n=35	n=20	n=15	n=35	n=20	n=15
General	1.59 (n=34)	1.58 (n=19)	1.60	1.54	1.70	1.33
Upper denture	1.50 (n=34)	1.60	1.36 (n=14)	1.60	1.65	1.53
Lower denture	1.54	1.60	1.47	1.57	1.80	1.27
Appearance	1.37	1.45	1.27	1.46	1.60	1.27
Retention	1.43	1.45	1.40	1.43	1.60	1.20
Functional comfort	1.60	1.70	1.47	1.51	1.70	1.27
Eating	2.54	3.05	1.87 c	2.12 (n=32)	2.47 (n=17)	1.73 d
Speaking	2.14	2.25	2.00	1.91 (n=34)	2.05 (n=19)	1.73

Survivors at T3 (n=20)								
T1			T2			T3		
total	RTX	n-RTX	total	RTX	n-RTX	total	RTX	n-RTX
n=20	n=9	n=11	n=20	n=9	n=11	n=20	n=9	n=11
General	1.65	1.44	1.82	1.40	1.44	1.36	1.50	1.44
Upper denture	1.45	1.44	1.45	1.45	1.33	1.55	1.40	1.33
Lower denture	1.55	1.44	1.64	1.35	1.33	1.36	1.55	1.67
Appearance	1.30	1.22	1.36	1.35	1.33	1.36	1.20	1.22
Retention	1.50	1.44	1.55	1.30	1.33	1.27	1.50	1.78 a
Functional comfort	1.55	1.44	1.64	1.35	1.44	1.27 b	1.50	1.56
Eating	2.20	2.56	1.91	1.95	2.22	1.73	1.70 e	1.78 e
Speaking	2.05	2.00	2.09	1.65	1.56	1.73	1.75	2.00

Data are depicted for the survivors at T2 and T3, respectively.

*1 = very satisfied, 2 = satisfied, 3 = neutral, 4 = dissatisfied, and 5 = very dissatisfied

a Significant difference between five years and one year after placement $p < 0.05$

b Significant difference between one year and 6 weeks after placement $p < 0.05$

c Significant difference between irradiated and non-irradiated patients at the same point in time $p < 0.01$

d Significant difference between irradiated and non-irradiated patients at the same point in time $p < 0.05$

e Significant difference between five years and 6 weeks after placement $p < 0.05$

RTX: irradiated patients, n-RTX: non-irradiated patients

Table 4. Overall denture satisfaction rate (range 0–10; 0 = completely dissatisfied and 10 = completely satisfied). Data are depicted for the survivors at T2 and T3, respectively

	T1	T2	T3
Survivors at T2			
Total n=35	8.0 ± 1.6	7.9 ± 1.8	deceased
RTX n=20	7.5 ± 1.6	7.5 ± 1.9	deceased
n-RTX n=15	8.6 ± 1.5	8.5 ± 1.4	deceased
Survivors at T3			
Total n=20	8.3 ± 1.5	8.5 ± 1.3	8.7 ± 1.2
RTX n= 9	8.1 ± 1.4	8.4 ± 1.2	8.6 ± 1.3
n-RTX n=11	8.5 ± 1.6	8.5 ± 1.4	8.9 ± 1.1

RTX: irradiated patients, n-RTX: non-irradiated patients

Table 5. Chewing Ability (range 0-2; 0 = good, 1 = moderate, 2 = bad)

	Survivors at T2 (n=35)					
	T1		T2			
	total n=35	RTX n=20	n-RTX n=15	total n=31	RTX n=16	n-RTX n=15
Soft food	0.50	0.72	0.20 ¹	0.38	0.57	0.18
Tough food	0.90	1.25	0.44 ²	0.72	0.98	0.44 ¹
Hard food	1.32	1.43	1.18	1.04 ^a	1.23	0.84 ^b

	Survivors at T3 (n=20)								
	T1			T2			T3		
	total n=20	RTX n=9	n-RTX n=11	total n=20	RTX n=9	n-RTX n=11	total n=18 (n=19)	RTX n=8 (n=9)	n-RTX n=10
Soft food	0.33	0.52	0.18	0.35	0.63	0.12	0.36 (n=19)	0.57 (n=9)	0.17
Tough food	0.67	1.00	0.39	0.60	0.85 ^a	0.39	0.62	0.67	0.60
Hard food	1.13	1.07	1.18	0.87 ^a	1.00	0.76 ^a	0.81	0.88	0.77

Data are depicted for the survivors at T2 and T3, respectively.

^a Significant difference between one year and 6 weeks after placement p<0.05

^b Significant difference between one year and 6 weeks after placement p=0.01

¹ Significant difference between irradiated and non-irradiated patients at the same point in time p< 0.05

² Significant difference between irradiated and non-irradiated patients at the same point in time p< 0.01

RTX: irradiated patients, n-RTX: non-irradiated patients

Denture satisfaction was considered as good, with the least favourable scores on eating and speaking at all evaluations (Table 3). Irradiated patients were more satisfied concerning eating with their dentures at T3 than at T1 (Wilcoxon signed ranks test, z=-2.332, P=0.02). However, between T2 and T3, the reported retention of their dentures had decreased. The non-irradiated patients were more satisfied with the functional comfort of their dentures at T2 than at T1. For the 1-year survivors at 6 weeks and 1 year after placement of the dentures, the irradiated patients reported more difficulty with eating than the non-irradiated patients (data not shown, for details see Schoen et al. 2008).

The overall denture satisfaction was high and did not differ between different evaluation points for the irradiated and non-irradiated patients (independent t-test, $P>0.05$). Also, there was no difference in overall denture satisfaction between irradiated and non-irradiated patients (Table 4, independent t-test, $P>0.05$). The reported chewing ability of hard food improved for the non-irradiated patients and irradiated patients who survived T3 between T1 and T2 (Table 5).

Discussion

This study showed a high percentage of rehabilitated patients with a functioning implant-retained mandibular overdenture 5 years after placement of the overdenture. One year after placement of the dentures 92% and after 5 years 83% of the surviving patients were functioning with their overdentures. In addition, we found a high overall survival rate of 92.8% of the implants in these patients and healthy peri-implant tissues. Patients were satisfied with their prosthesis, even though the chewing ability was impaired. A wide variety in the percentages (22–91%) of patients who completed prosthetic treatment after head and neck oncology treatment has been reported in the literature (Rogers et al. 2005; Garrett et al. 2006; Schepers et al. 2006; Nelson et al. 2007; Schoen et al. 2007; Hundepool et al. 2008; Adell et al. 2008; Smolka et al. 2008). This variation in percentages was heavily depending on the type of patients included, the type of reconstruction, the survival rate of patients and implants and the follow-up. A main advantage of installing implants during ablative surgery seemed to be the high percentage of rehabilitated patients and the time reduction for (pre)prosthetic rehabilitation. Regarding implant installation after oncological treatment, for many patients, the anticipated benefits of an implant-retained overdenture often did not outweigh the burden of another surgical intervention. An additional disadvantage of implantation during ablative surgery, which has to be mentioned, is the risk that implants will not be used due to patients refusing the abutment connection operation and thus refrain from prosthetic rehabilitation ($n=3$ in this study), or tumour-related death or death because of other reasons ($n=7$ in this study). Patients with severe comorbidity or higher tumour stages might show less long-time survival. However, this group is also thought to have less favourable anatomic conditions after treatment and therefore was supposed to benefit the most and as early as possible from implant support to be able to function with their prostheses. From a health economics point of view, the loss of resources needs more detailed analyses. Funding of care seems an important decisive factor as funding might be related to survival of the patients. Some jurisdictions will fund care irrespective of expected duration of survival of the patients, while others do not fund care until after 2 years of survival or even delay funding to 5-year survival. In the Dutch health care funding system, the cost of rehabilitation is taken care of irrespective of the prognosis of the patient. These various jurisdictions create a tremendous ethical dilemma and particularly so for clinicians

providing care where managed or public funding is applied. We feel that funding should be made available irrespective of the predicted survival of the patients. Which care the patients should be provided with, should be dependent on professionals' opinion aiming for early restoration of oral functioning where judged feasible for a particular patient. In other words, whether implant treatment is indicated in a particular patient should be based on the complex of expected benefits in that patient taking the expected survival of the patient in consideration too (the patient should be able to benefit of the treatment) and not be predominantly directed by funding jurisdictions.

Implant survival was higher in patients who did not receive radiotherapy after tumour surgery. This is in agreement with other studies (Granström 2003, 2005; Yerit et al. 2006; Colella et al. 2007; Idhe et al. 2009). In addition, we observed more late loss of implants in our study (Fig. 2). However, a failure rate of 10.6% in irradiated bone over a period of 5 years is considered good. After 5 years, 26 patients had died; these patients were excluded from the survival analyses for those evaluation time points that were not complete (in none of these patients additional implants had been lost between the last evaluation and the date they passed away). Also, the percentage of patients who had received postoperative radiotherapy decreased over time among the survivors (73% at baseline versus 54% 5 years after placement of the dentures). This could have contributed to the relatively low failure rate of implants in irradiated bone.

The clinical variables assessed in our study were low at all evaluations, showing a good peri-implant health. These findings were comparable with findings in healthy subjects (Meijer et al. 2004, 2009; Visser et al. 2005). This can be the result of the strict oral hygiene regime to which patients were subjected. However, in a few patients with the tumour located in the ventral part of the floor of the mouth, and who received soft tissue flaps adjacent to the implant site, lasting soft tissue problems were seen, due to mobility and thickness of the skin (n=3 in this study). In this type of patients, soft tissue problems have to be anticipated on beforehand.

Rotational panoramic radiographs are widely used in the evaluation of bone around the implants, although they lack sharpness, distort images and superimpose bony structures of the spine (Meijer et al. 1992). Reproducibility is difficult to achieve. The score used in this study (Geertman et al. 1996) can be seen as a rough estimation of the bone level, suitable for comparison of relatively large differences. Bone loss is to be expected after implant installation, as defined by Adell et al. (1981) and Albrektsson et al. (1986), but no statistical significant differences were observed in bone levels around irradiated implants and non-irradiated implants. It is possible that this is the result of the measuring method. Late implant loss was higher in irradiated patients, which may point to a more severe bone loss in irradiated patients. As the peri-implant tissues remained healthy and the implants were still in use for the implant-retained overdenture, there were no clinical consequences. In the future, however, it is imaginable that implants with higher levels of bone loss are yet suspect to being lost.

Denture satisfaction was considered very high, comparable with the level reported for healthy subjects (Stellingsma et al. 2003), which is surprising, because the oral condition in these oral cancer patients was compromised. However, denture satisfaction was measured of the 20 patients with a functioning prosthesis after 5 years, which might be a more favourable result than would apply for the total group of living patients at T3 (n=24). The subjective chewing ability did not reach the same level as seen in healthy subjects (Stellingsma et al. 2005). The oral function is compromised in oral cancer patients, as a result of the oncological surgery and, when necessary, additional radiotherapy. Irradiated patients seemed to have more difficulty chewing tough food, perhaps due to hyposalivation and its related complaints resulting from radiotherapy. This difference, however, was not present 5 years after placement of the dentures, which might be due to recovery of the early (mainly mucosal) effects of radiotherapy and patients becoming adjusted to their oral condition. However, patients with a feeding tube or patients who did not wear their dentures while eating (n=2 at T3) did not complete this questionnaire, which might have resulted in more favourable results as well. Tang et al. (2008) indicated in their review that implant-retained prosthetic rehabilitation resulted in the most favourable masticatory outcomes, when compared with no prosthetic treatment or conventional prosthetic treatment. It is probable that, without implant-retained overdentures, the patients in our study would have reported even worse scores on chewing ability.

From this study, it is concluded that the percentage of patients with successful prosthetic treatment with an implant-retained overdenture was high with the implants installed during ablative surgery. In addition, survival rate of implants installed during ablative surgery is high, although the survival rate in irradiated bone is less than in non-irradiated bone. When oral rehabilitation can be established with an implant-retained overdenture in the mandible, satisfaction levels remained high during the 5-year follow-up.

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Chapter 2.3

Overdentures on primary
mandibular implants in patients
with oral cancer: a follow up
study over 14 years

Abstract

Objectives

We aimed to assess oral functioning, patients' satisfaction, condition of peri-implant tissues, and survival of implants up to 14 years after their insertion in patients with oral cancer who had had mandibular overdentures placed over primary implants.

Materials and methods

Endosseous dental implants were inserted prospectively in the interforaminal region of the mandible during resection of the tumour in 164/180 patients with oral cancer. All 58 patients were evaluated by questionnaires and clinical assessments during a final assessment in 2012.

Results

In 84% of the patients an implant-retained mandibular overdenture was inserted. Completion of prosthetic rehabilitation and oral functioning was not associated with primary site or stage of the tumour, number or type of implants inserted, or the type of reconstruction. Over time the peri-implant mucosa was usually free of inflammation. More implants were lost in irradiated patients (8.5%) than in non-irradiated patients (0.5%). Irradiated patients reported more problems in oral functioning and less satisfaction than non-irradiated patients. Patients with an implant-retained mandibular overdenture reported fewer problems in oral functioning than patients without an overdenture.

Conclusion

Primary implant insertion in oral cancer patients should be routinely incorporated in the surgical planning as oral functioning in patients wearing mandibular overdentures improves considerably and peri-implant health is at least reasonable.

Introduction

Surgical tumour resection in the oral cavity can have a profound effect on oral functions such as chewing, swallowing and intelligible speech¹. Postoperative radiotherapy usually further compromises oral functioning. Changes in oral anatomy due to surgery and sequelae from radiotherapy such as xerostomia and intolerance of the denture-bearing mucosa to mechanical loading limit prosthetic rehabilitation of these patients². As a result, prosthetic rehabilitation of edentulous oral cancer patients is difficult and therefore often omitted. However, adequate prosthetic rehabilitation is a pivoting factor for patients to regain oral functions³.

In healthy patients oral function can be improved using implant-retained mandibular overdentures^{4,5}. This treatment has evolved into an important asset in the rehabilitation of oral cancer patients as well⁶. Insertion of implants may be best during the ablative surgery (primary implant insertion)⁷⁻¹¹ as it has been shown that many patients postpone or simply decline an offered implant-based treatment after tumour surgery and postoperative radiotherapy¹²⁻¹⁴.

Primary implant insertion appreciably reduces time between tumour surgery and prosthetic rehabilitation. This may allow patients to better and earlier regain their oral function after completion of the oncologic treatment. Another advantage is the presumed higher survival rate of the implants when implants are inserted before the radiotherapy instead of after radiotherapy, as initial osseointegration will have taken place before implants and mandibular bone are exposed to ionising radiation. Systematic reviews showed that most publications on dental implants in oral cancer patients referred to implants inserted after the surgery and/or radiotherapy had been completed, while only a very limited number of studies reported on primary implants^{15,16}. We presume that the benefits of primary insertion outweigh the risk the implants will not be used for prosthetic rehabilitation. However, further study is needed to estimate which oral cancer patients can benefit from primary implants. Does it depend on the primary location of the tumour, its size, if the patient is irradiated or the type of reconstructive surgery?

In this study, we have assessed treatment outcomes (which patients benefit, their quality of life, their oral functioning and satisfaction, the condition of peri-implant tissues and implant survival) in a prospective cohort of 164 oral cancer patients with primary mandibular implants to support an implant-retained mandibular overdenture up to 14 years after insertion of the implants.

Patients and methods

Patient inclusion criteria and treatment

All consecutive edentulous patients with oral cancer referred to the Head and Neck Oncology group of the University Medical Center Groningen between May 1998 and November 2010 were screened to be included in this study. Inclusion criteria were:

- edentulous upper and lower jaw;
- history of prosthetic problems related to lack of stability and retention of the lower denture or expected lower denture-related problems after oncologic treatment;
- malignancy in lower oral cavity region or oropharynx (squamous cell carcinoma of tongue, floor of the mouth, mandibular gingiva, buccal mucosa, lower lip, or tonsil) with the need for primary curative ablative surgery;
- little or no improvement expected from making new dentures after oncological treatment.

At the inclusion, all patients were offered a choice of conventional or implant-based treatment. Tumour surgery, implant insertion and prosthetic treatment were performed at the University Medical Center Groningen. The implants were 3.75 mm Brånemark implants (Nobelbiocare, Gothenburg, Sweden), either with a machined surface (before September 2003) or a Ti-Unite® surface (from September 2003). All implants were inserted in the interforaminal region of the native bone of the mandible immediately after the ablative tumour surgery procedure. Implant insertion and abutment placement were planned as a two-stage surgical procedure. Depending on the available bone and prosthetic demands 2, 3 or 4 implants were inserted.

A 3-months osseointegration period before abutment placement was considered in patients not subjected to radiotherapy after tumour surgery. In patients that were subjected to postoperative radiotherapy or chemoradiation, radiotherapy started in general within 6 weeks after surgery. The osseointegration time before abutment placement in irradiated patients was increased to at least 9 months after surgery, i.e. 6 months after completion of radiotherapy, according to Schoen et al⁹. After abutment placement, an implant-retained overdenture was made.

Clinical assessments

Postoperative complications and implant survival were recorded from the time of surgery until March 2012. Periodontal indices were assessed during a final assessment in 2012 according to Schoen et al⁹. Patients in whom prosthetic rehabilitation was completed less than one year before assessment were excluded from this analysis.

Radiographic evaluation

Marginal bone resorption for the implants was assessed using panoramic radiographs, where the bone level was calculated in relation to the implant shoulder.

Quality of life, functional assessments and denture satisfaction

During a final assessment in 2012, quality of life, oral function and denture satisfaction were assessed using validated questionnaires. Again, patients in whom prosthetic rehabilitation was completed less than one year before assessment were excluded from this analysis. Quality of life (QoL) was assessed using the core questionnaire (QLQ-C30) and head and neck module (QLQ-H&N35) of the European Organization for Research and Treatment of Cancer (EORTC)¹⁷.

Denture satisfaction was assessed using a validated questionnaire consisting of 8 separate items focusing on the function of upper and lower dentures, and on specific features such as aesthetics, retention and functional comfort¹⁸. Overall denture satisfaction was expressed on a 10-point rating scale. Subjective chewing ability was assessed using a 9-item questionnaire on which the patient could rate on a 3-point scale their ability to chew different kinds of food⁵. Psychological, physical and social impact of oral disorders was assessed using the Oral Health Impact Profile (OHIP)¹⁹.

Data analysis

The data were evaluated using SPSS (IBM SPSS Statistics, version 20, Armonk, NY). For non-parametric data (4 items of the EORTC QLQ-C30: emotional functioning, cognitive functioning, social functioning and pain) Mann-Whitney and Kruskal- Wallis tests were used. For parametric data (all other variables) independent t-tests and one way ANOVA were used.

For testing the distribution among groups the Fisher's exact test was used for comparing two different groups and the chi square test was used for several different groups. Generalized Estimating Equation models were made using Stata IC version 11.0 (StataCorp,Texas USA). For all statistical analyses α was set at 0.05.

Results

Patients and implants

One hundred and eighty patients fulfilled the inclusion criteria. In 15 patients no implants were inserted due to anatomical limitations of the mandible that appeared or were created during ablative surgery, such as lack of bone volume for implant insertion. One patient had chosen conventional treatment instead of implant insertion. Thus, a total of 16 patients were excluded for analyses. Patient selection is depicted in Figure 1. The characteristics of the study group are presented in Table 1.

Figure 1. Algorithm showing selection of patients. The light blue boxes represent the patients' status during the final recall in 2012

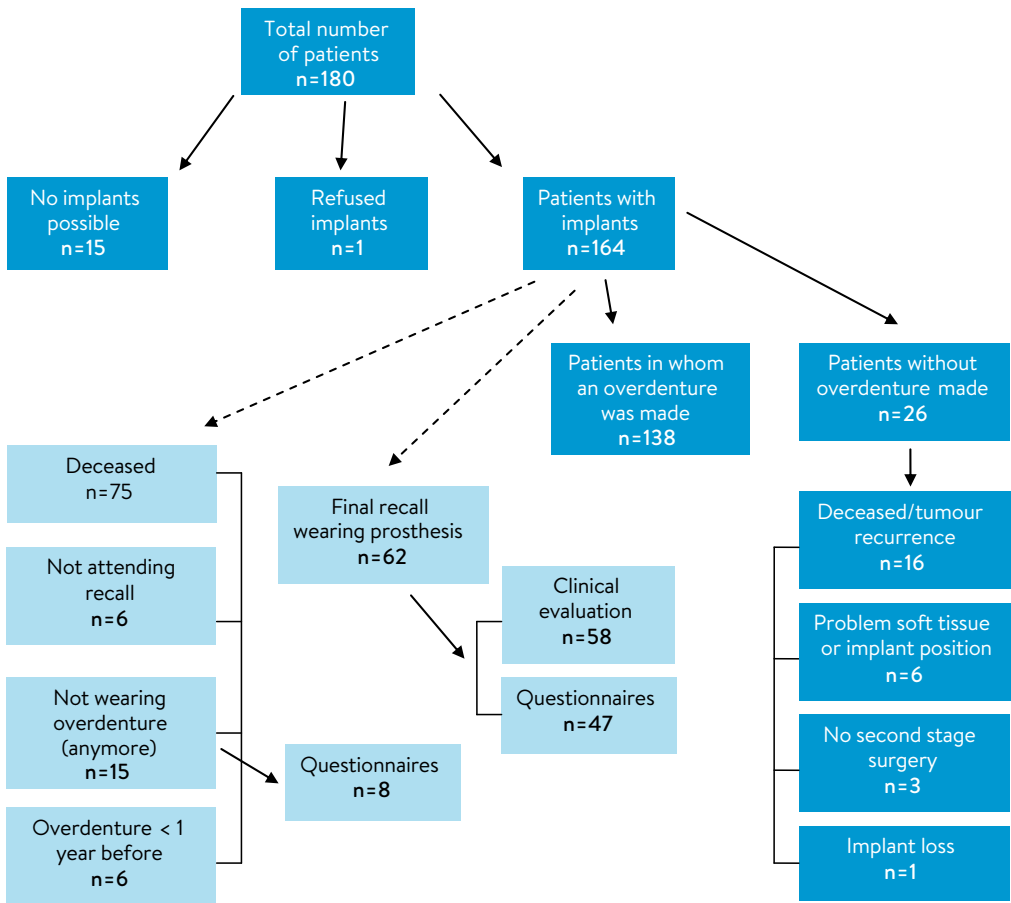


Table 1. Characteristics of the study group (RTX= in irradiated patients, n-RTX= in non- irradiated patients)

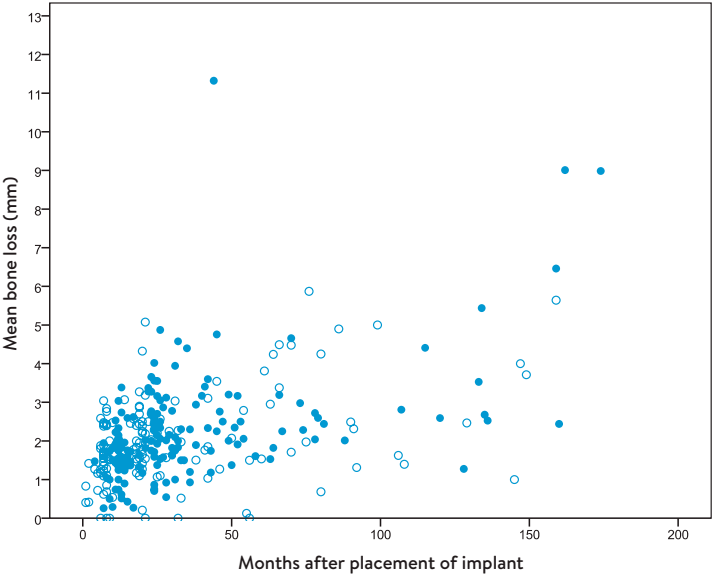
Patients	
Total number	164
Gender (number male/ female)	98/ 66
Mean age at time of surgery in years (SD, range)	64.8 (10.9, 39-88)
Tumour UICC stage I (number of patients)	35
Tumour UICC stage II (number of patients)	40
Tumour UICC stage III (number of patients)	40
Tumour UICC stage IV (number of patients)	49
Smoking/non-smoking/unknown (number of patients)	91/ 65/ 8
Radiotherapy (number irradiated/ non-irradiated)	100/ 64
Median follow-up in years (range)	3.8 (0-14.5)
Patients with 2/3/4 implants	62/ 8/ 94
Patients with overdenture (percentage)	138 (84.2%)
Median time between surgery- prosthesis placement in months RTX (range), n=81	11.3 (5.1-64.2)
Median time between surgery- prosthesis placement in months n-RTX (range), n=57	6.3 (4.2-18.7)
Median time prosthesis was worn in years (range)	3.1 (0-13.4)
Implants	
Total number	524
Radiotherapy (number irradiated/ non-irradiated)	318/ 206
Number of lost implants RTX/n-RTX (percentages)	31/ 5 (9.4%/ 2.4%)
Implants lost without implants lost due to resection of recurrent tumour RTX/n-RTX (percentages)	27/ 1 (8.5%/ 0.5%)

Loss of implants in this cohort was higher in irradiated patients than in non-irradiated patients, when excluding implants lost due to resection of recurrent tumour 8.5% versus 0.5% of the implants respectively (Fisher's exact $p < 0.001$). Implant loss was not associated with smoking at the time of the intake. Furthermore, implant loss in irradiated patients was not dependent on the implant surfaces applied, viz. a Ti-unite surface (16 out of 153 implants) or a machined surface (11 out of 165 implants; Fisher's exact $p = 0.318$).

Osteoradionecrosis (ORN) located in proximity of the implants was observed in 5 patients. Ten implants were removed combined with a sequestrectomy. Three patients received additional hyperbaric oxygen (HBO). In 4 patients treatment of ORN was successful; 1 patient appeared to have a tumour recurrence with pathological fracture of the mandible in the area of the ORN. Smoking at time of intake was not associated with the occurrence of ORN. No valid data were available whether or not the patients continued their smoking habits after treatment.

Bone loss around the implants increased significantly over time, both in irradiated as in non-irradiated patients (Fig 2). There was no significant bone loss in irradiated patients compared to in non-irradiated patients (Longitudinal data analysis, GEE model, $p = 0.649$).

Figure 2. Mean bone loss (difference between bone level and the implant shoulder) in mm for irradiated patients (filled dots) and non-irradiated patients (outlined dots) over time



In 26 patients (16%) prosthetic rehabilitation was not completed for a number of reasons (Fig 1). Completion of prosthetic rehabilitation was not associated with radiotherapy ($p=0.388$) or type of implants inserted ($p=0.828$, both Fisher's exact), tumour location ($p=0.199$), the number of implants ($p=0.965$), type of surgical reconstruction used during tumour surgery ($p=0.063$) and tumour stage ($p=0.119$, all chi square test).

Clinical assessments

The median periodontal indices showed reasonably healthy peri-implant mucosa (Table 2).

Table 2. Periodontal indices of the patients during final recall in 2012

	N	Median (25%-75%)
Plaque index (score 0 to 3)	58	1.00 (0.31-1.54)
Calculus (score 0 or 1)	58	0.00 (0.00-0.54)
Bleeding index (score 0 to 3)	58	1.29 (0.75-1.50)
Gingiva index (score 0 to 3)	58	0.29 (0.00-1.00)
Pocket depth (mm)	57	2.81 (2.37-3.25)
Width of attached gingiva (score 0-3)	58	2.25 (1.63-2.78)

Quality of life, functional assessments and denture satisfaction

Irradiated patients reported more insomnia, more problems with social eating, more problems with mouth opening, more limitations of oral function, and less satisfaction than non-irradiated patients (Table 3).

Table 3. Results of EORTC QLQ-C30, EORTC QLQ-H&N 35, Oral Health Impact Profile (OHIP), denture satisfaction and subjective chewing ability questionnaires during final recall in 2012, 1.5-14.5 years postoperatively. (RTX= irradiated, n-RTX= non-irradiated, MW= Mann-Whitney test)

	RTX (n=35) Mean±SD	nRTX (n=23) Mean±SD	Statistic test	95 % confidence Lower	interval Upper	t	df	p-value
EORTC QLQ-C30								
Global health status/QoL	80.5±16.3	75.4±21.1	T-test	-14.97	4.75	-1,04	56	0.30
Physical function	79.8±19.9	70.4±23.2	T-test	-13.44	52.35	1,76	57	0.085
Role function	79.0±26.6	75.4±32.1	T-test	-11.86	19.23	0.48	56	0.64
Emotional function	88.3±17.6	77.5±29.7	MW					0.16
Cognitive function	87.6±16.8	85.5±23.7	MW					0.98
Social function	85.3±21.2	86.2±31.2	MW					0.24
Fatigue	22.1±23.3	26.1±25.6	T-test	-8.94	16.98	0.62	57	0.54
Nausea / vomiting	1.4±8.3	6.5±14.0	T-test	-1.44	11.71	1.59	32.08	0.12
Pain	15.7±23.6	17.4±29.5	MW					0.89
Dyspnoea	15.7±25.8	30.4±31.6	T-test	-29.77	0.38	-1.95	57	0.056
Insomnia	10.2±19.2*	29.0±35.3*	T-test	-35.17	-2.43	-2.35	30.46	0.026
Appetite loss	12.0±27.8	11.6±25.8	T-test	-14.01	14.90	0.061	57	0.95
Constipation	7.6±21.5	14.5±28.1	T-test	-19.95	6.21	-1.05	56	0.30
Diarrhoea	2.9±12.4	8.7±18.0	T-test	-14.58	2.90	-1.36	35.68	0.18
Financial problems	4.9±14.5	8.7±25.1	T-test	-14.31	6.72	-0.72	55	0.47
EORTC QLQ-H&N35								
Pain	14.3±16.1	18.6±27.6	T-test	-8.954	17.50	0.66	30.13	0.51
Swallowing	21.6±22.7	15.1±29.8	T-test	-20.65	7.63	-0.92	54	0.36
Senses	19.0±24.3	17.4±27.4	T-test	-15.55	12.31	-0.23	55	0.82
Speech	17.8±20.4	14.7±22.6	T-test	-14.72	8.50	-0.54	54	0.59
Social eating	28.5±31.3*	12.1±22.2*	T-test	-31.91	-0.92	-2.12	53	0.038
Social contact	8.7±16.5	9.0±18.8	T-test	-9.26	9.75	0.052	54	0.96
Sexuality	30.0±37.6	52.2±40.3	T-test	-3.29	47.74	1.763	38	0.086
Teeth	16.7±25.4	14.3±27.0	T-test	-12.30	17.07	0.33	51	0.75
Opening mouth	36.2±35.6*	18.2±28.6*	T-test	-0.03	36.05	2.00	55	0.050
Dry mouth	45.7±33.4	31.8±36.3	T-test	-4.95	32.74	1.48	55	0.15
Sticky saliva	28.6±36.3	21.2±35.0	T-test	-12.15	26.87	0.76	55	0.45
Coughed	17.1±23.4	18.2±26.7	T-test	-14.51	12.43	-0.16	55	0.88
Felt ill	9.5±17.3	15.2±32.1	T-test	-20.85	9.59	-0.76	28.77	0.46
Pain killers	28.1±45.7	47.8±51.1	T-test	-46.63	7.23	-1.47	44.20	0.15
Nutritional support	30.3±46.7	17.4±38.8	T-test	-10.08	35.90	1.13	52.25	0.27
Feeding tube	6.1±24.2	4.3±20.9	T-test	-10.77	14.19	0.28	54	0.78
Weight loss	15.2±36.4	21.7±42.2	T-test	-27.75	14.58	-0.62	54	0.54
Weight gain	24.2±43.5	30.4±47.0	T-test	-30.69	18.31	-0.51	54	0.61
OHIP								
OHIP14	17.4±12.6	14.4±15.2	T-test	-0.80	2.96	1.31	57	0.19
Functional limitation	13.3±6.8*	8.7±6.6*	T-test	0.88	8.15	2.49	56	0.016
Physical pain	8.3±5.9	7.5±7.5	T-test	-2.61	4.35	0.50	58	0.62
Physical disability	13.3±8.5	8.8±9.4	T-test	-0.26	9.20	1.89	57	0.063

Psychological discomfort	4.4±4.4	4.0±5.6	T-test	-2.21	2.93	0.28	58	0.78
Psychological disability	3.7±4.1	4.3±6.6	T-test	-3.73	2.38	-0.45	35.07	0.66
Social disability	2.6±3.3	3.2±5.4	T-test	-2.83	1.76	-0.46	56	0.65
Denture satisfaction								
Denture satisfaction (range 8-40)	15.4±5.7	13.0±4.2	T-test	-0.55	5.38	1.64	49	0.11
Overall denture satisfaction (range 0-10)	7.4±1.4*	8.1±0.9*	T-test	-1.38	-0.095	-2.30	50.76	0.025
Chewing/ eating (range 0-18)	8.9±6.1	6.6±6.2	T-test	-1.08	5.76	1.37	54	0.18

* p<0.05

Chewing ability and several items reflecting oral functioning of the EORTC QLQ-C30 and QLC-H&N35 and OHIP were significantly worse for patients not wearing an implant-retained mandibular overdenture on the implants (Table 4).

Table 4. Results of EORTC QLQ-C30. EORTC QLQ-H&N 35. Oral Health Impact Profile (OHIP). denture satisfaction and subjective chewing ability questionnaires during final recall in 2012, 1.5-14.5 years postoperatively. (Proth= patient wearing an implant-retained mandibular overdenture. nproth= patient not wearing an implant-retained mandibular overdenture)

	proth (n=51) Mean±SD	nproth (n=8) Mean±SD	Statistic test	95 % confidence Lower	interval Upper	t	df	p-value
EORTC QLQ-C30								
Global health status/QoL	79.6±18.2	70.2±18.5	T-test	-24.07	5.39	-1.27	56	0.21
Physical function	77.6±19.6	66.7±31.3	T-test	-31.79	56.75	1.05	57	0.30
Role function	79.7±26.4	64.6±40.3	T-test	-18.87	49.04	1.03	8.00	0.34
Emotional function	84.6±24.0	79.8±20.9	MW					0.39
Cognitive function	87.3±19.9	83.3±19.2	MW					0.53
Social function	88.3±23.4*	66.7±33.3*	MW					0.04
Fatigue	22.7±24.2	29.9±23.9	T-test	-11.22	25.63	0.78	57	0.44
Nausea / vomiting	3.9±11.8*	0.0±0.0*	T-test	-7.248	-0.60	-2.37	50.00	0.02
Pain	18.0±27.0	6.3±12.4	MW					0.27
Dyspnoea	20.9±27.5	25.0±38.8	T-test	-26.24	18.07	-0.37	57	0.71
Insomnia	19.0±29.3	8.3±15.4	T-test	-10.65	31.89	1.00	57	0.32
Appetite loss	9.8±25.2	25.0±34.5	T-test	-35.39	5.00	-1.51	57	0.14
Constipation	11.1±25.5	4.8±12.6	T-test	-13.41	26.11	0.644	56	0.52
Diarrhoea	3.9±12.7	14.3±26.2	T-test	-34.65	13.92	-1.03	6.39	0.34
Financial problems	6.0±18.7	9.5±25.2	T-test	-19.29	12.24	-0.45	55	0.66
EORTC QLQ-H&N35								
Pain	16.7±22.0	10.7±13.4	T-test	-23.13	11.23	-.69	55	0.49
Swallowing	18.0±25.9	28.7±21.7	T-test	-11.41	32.81	0.97	54	0.34
Senses	18.0±26.5	21.4±15.9	T-test	-17.22	24.08	0.33	55	0.74

Speech	13.9±20.1*	34.9±20.7*	T-test	4.64	37.31	2.57	54	0.013
Social eating	18.1±26.6†	48.8±32.4†	T-test	8.59	52.92	2.78	53	0.007
Social contact	5.9±12.3	29.8±30.8	T-test	-4.59	52.41	2.03	6.28	0.086
Sexuality	38.7±38.9	33.3±57.7	T-test	-54.15	43.34	-0.22	38	0.82
Teeth	16.0±26.3	11.1±19.2	T-test	-26.20	35.97	0.32	51	0.75
Opening mouth	26.0±31.8‡	52.4±42.4‡	T-test	-53.17	0.40	-1.97	55	0.053
Dry mouth	40.0±35.0	42.9±37.1	T-test	-31.35	25.63	-0.20	55	0.84
Sticky saliva	22.7±33.3	47.6±46.6	T-test	-53.25	3.34	-1.77	55	0.083
Coughed	15.3±23.5	33.3±27.2	T-test	-37.38	1.38	-1.86	55	0.068
Felt ill	11.3±24.8	14.3±17.8	T-test	-22.51	16.60	-0.30	55	0.76
Pain killers	37.5±48.9	28.6±48.8	T-test	-30.76	48.62	0.45	53	0.65
Nutritional support	22.4±42.2	42.9±53.5	T-test	-55.69	14.88	-1.16	54	0.25
Feeding tube	4.1±20.0	14.3±37.8	T-test	-45.21	24.80	-0.70	6.49	0.51
Weight loss	16.3±37.3	28.6±48.8	T-test	-43.66	19.17	-0.78	54	0.44
Weight gain	28.6±45.6	14.3±37.8	T-test	-22.04	50.61	0.79	54	0.43
OHIP								
OHIP14	14.2±12.8†	29.3±12.6†	T-test	-0.59	-0.18	-4.00	17.80	0.001
Functional limitation	10.5±6.9†	19.5±1.6†	T-test	-11.33	-6.59	-7.70	32.45	0.000
Physical pain	7.7±6.6	9.7±6.0	T-test	-7.01	3.00	-.81	58	0.42
Physical disability	9.9±8.3†	22.0±6.4†	T-test	-18.31	-6.00	-3.96	57	0.000
Psychological discomfort	3.4±3.9*	9.8±7.0*	T-test	-12.24	-0.53	-2.53	7.67	0.036
Psychological disability	3.4±4.9*	7.5±6.1*	T-test	-7.95	-0.30	-2.16	57	0.035
Social disability	2.3±3.7†	6.6±5.6†	T-test	-7.36	-1.25	-2.82	56	0.007
Denture satisfaction								
Denture satisfaction (range 8-40)	14.2±5.2							
Overall denture satisfaction (range 0-10)	7.7±1.3							
Chewing/eating (range 0-18)	7.0±5.9	15.3±2.7	T-test	-11.08	-5.49	-6.28	16.11	0.000

* p<0.05

† p<0.01

‡ p=0.053

No differences were seen in oral function, chewing ability and satisfaction between the different tumour stages and tumour locations, between the different types of reconstruction used during tumour surgery, or between the number of implants inserted during the ablative surgery (ANOVA, $p>0.05$ and Kruskal- Wallis, $p>0.05$, results not shown).

Discussion

Many edentulous oral cancer patients may benefit from insertion of endosseous dental implants during ablative surgery at an early stage after ablative tumour surgery. Completion of prosthetic rehabilitation and oral functioning, chewing ability and satisfaction were independent of tumour location, tumour stage, type of reconstruction used during ablative surgery and the number of implants inserted. Patients wearing an implant-retained mandibular overdenture had significantly better chewing ability, less social disability and better oral functioning than patients not wearing an overdenture. Furthermore, patients that did not undergo postoperative radiotherapy had higher scores for satisfaction and oral functioning than irradiated patients. Implant loss was higher in irradiated patients than in non-irradiated patients.

Mizbah et al.¹⁴ compared patients with implants inserted during ablative surgery with patients that received implants postponed. They showed that patients with primary implants had their implant-retained overdenture on average after 7.4 months, while patients that received implants postponed received their overdenture after 27.4 months. In this study the median time between implant insertion and prosthesis placement was 11.3 months for irradiated patients and 6.3 months for non-irradiated patients. We used a minimal time-span of 6 months between the end of the radiotherapy and abutment placement, depending on the oral situation of the individual patient. The time between implant insertion and prosthetic rehabilitation can be reduced further, with shortening the time between completion of radiotherapy and abutment placement or by using one stage implants. However, it seems advisable to wait with abutment placement for the short-term side-effects of the radiotherapy such as mucositis to improve, e.g. 3 months at least. To our knowledge, no publications exist on one-stage implant insertion during ablative surgery. We hypothesize that this will yield similar results, also in patients that will be irradiated postoperatively, thus in most cases omitting the need of a second surgical intervention. Completing prosthetic rehabilitation and its outcome was not associated with tumour location. In 6 patients no implant-retained mandibular overdenture could be made due to improper implant positioning or because of problems with the peri-implant tissue related to the surgical treatment of the tumour. Noticeable was that in 5 out of these 6 patients the primary tumour was located in the ventral area of the floor of the mouth-the same area in which the implants were inserted. This can impede proper implant positioning as the anatomical situation and intermaxillary relationship are altered during surgery. Also it is more difficult to gain proper attached mucosa around the implants and retain a proper buccal and/or lingual vestibule to accommodate an overdenture (neutral zone). Oral functioning and patients' satisfaction was not associated with the number of implants inserted (2, 3 or 4 implants), as is comparable to previous studies in healthy subjects^{20, 21}. From a health- economics point of view, and from a patients' perspective of being able to perform proper oral hygiene in a compromised oral condition, inserting 2 implants during resection of the tumour seems advisable. A disadvantage of inserting 2 implants can be

that implant loss results in the patient not being able to wear an overdenture. In the 3 patients in our study in whom only one implant was left, it was still possible to provide an implant retained overdenture only attached to this one implant.

In this cohort study both short-term and long-term results were presented. Previous studies have shown that the outcome of quality of life and oral functioning questionnaires and patients' satisfaction remained stable between 1 and 5 years after prosthetic rehabilitation^{10, 11}.

Implant loss is inevitable, especially in irradiated patients, in whom survival rates reported in the literature vary largely^{15-16, 22}. In this study all implants were inserted in native mandibular bone by several consultants as well as residents. We therefore consider these results to be a reflection of what is achievable in routine care. ORN leading to implant loss was observed in 5 cases (5% of irradiated patients). This risk on developing ORN and implant loss is presumed to be higher when implants are inserted post radiotherapy. Comparison, however, is difficult since most studies have reported on implants placed after radiotherapy¹⁵. Primary implants can cause backscattering of radiation, resulting in an increased radiation dose in the surrounding bone in front of and next to the implants of 10-21%^{23, 24}. Whether this locally increased radiation dose can be the explanation for the observed higher implant loss in irradiated patients or a higher risk on developing ORN is not yet known, but presumably, even when this risk is increased, this risk will still be lower than for implants placed after radiotherapy.

Implant loss and ORN were not associated with smoking at the time of inclusion of the patients in this study. From the patients' records no reliable information could be retrieved whether patients continued their smoking habit after the oncological treatment or not. However, although it is probable that smoking has contributed to implant loss and occurrence of ORN, their contribution to these phenomena in the current study is considered to be low. Presumably, the leading factor in both implant loss and occurrence of ORN is radiotherapy.

From this study it is concluded that a large number of oral cancer patients in whom implants are inserted during the ablative surgery may benefit at an early stage from an implant-retained mandibular overdenture, with a good oral function, high prosthesis satisfaction and a low risk of implant loss. Implant insertion during ablative surgery in oral cancer patients should be routinely incorporated in the surgical planning.

Conflict of Interest

None declared

Ethics statement/confirmation of patient permission

None required

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Chapter 2.4

Mandibular implants placed during ablative tumour surgery— which patients can benefit?

Dear Editor,

We read the retrospective study of Mizbah et al.[1] on the comparison between oral cancer patients who received endosseous dental implants in the mandibular interforaminal area, either during ablative surgery or delayed, with great interest. We underline their conclusion that patients with the implants placed during ablative surgery will benefit earlier from an implant-retained mandibular overdenture than patients for whom implant placement is delayed, but feel that such a firm conclusion cannot be drawn on the basis of their study design and the analysis provided. In fact, their primary outcome measure, that patients provided with implants during ablative surgery will be subjected to earlier prosthetic rehabilitation without an increased complication rate, is a non issue. As patients for whom implant insertion was postponed had to show a recurrence-free interval of at least 1 year and next had to be subjected to hyperbaric oxygen treatment (HBO) and a longer osseointegration interval, one could expect that most of them would not have started with implant treatment at a date the other patients, with implants placed during the ablation, had already been provided with implant-retained overdentures. Furthermore, from a radio-biological perspective, the risk of developing a higher complication rate is unlikely, as the risk of developing, for example, osteoradionecrosis, will increase with the time elapsed after radiotherapy.

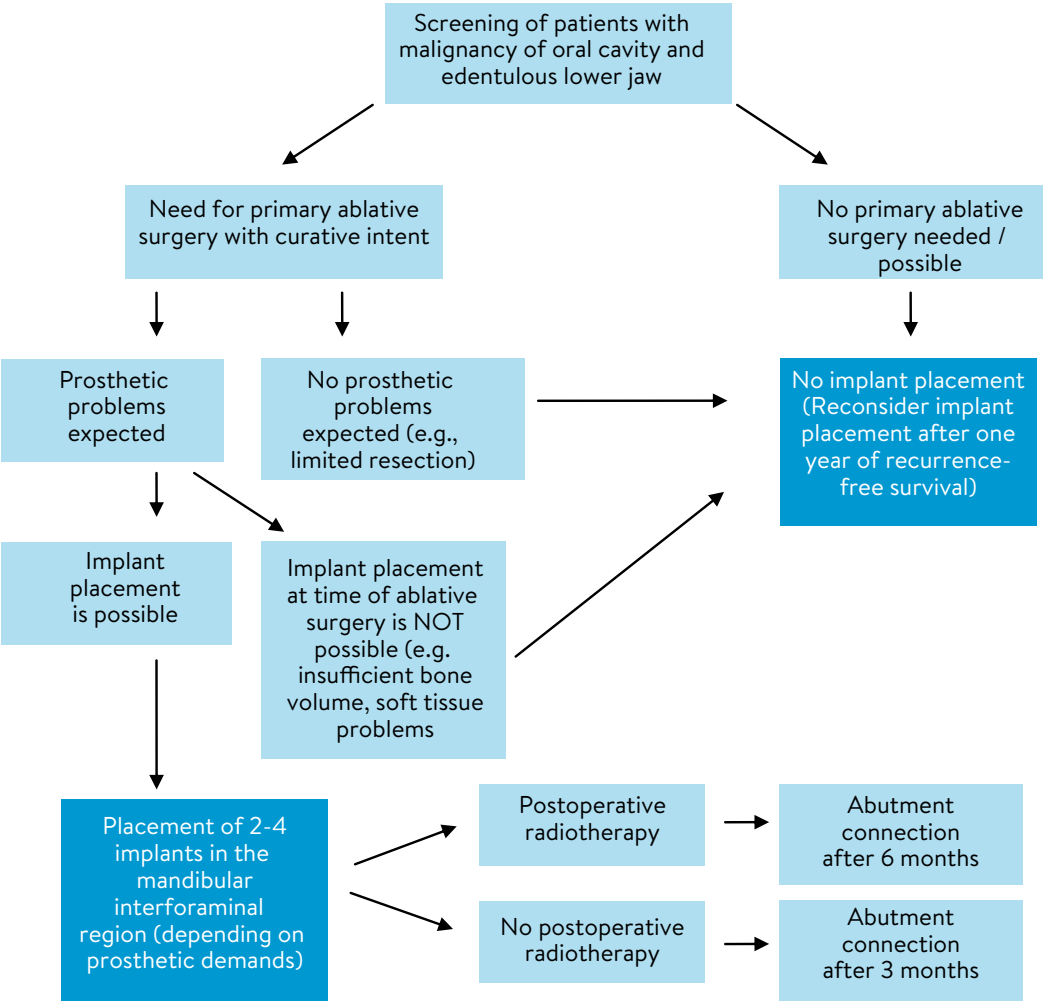
In contrast to what was reported in the prospective studies of, for example, Schoen et al.[2] and Korfage et al.[3, 4], no attempt was made to rate the functional outcome and quality of life using the different treatment protocols, although much attention was paid to this issue in the discussion.

In fact two different protocols applied at different centres were compared, which makes a comparison of the results impossible. What would have been the outcome had the treatments at the two centres been reversed? The same? Or would, for example, implant survival and the number of patients wanting implants later after tumour therapy be higher or lower? Furthermore, the need for HBO is not discussed; it is just standard care at the participating centre. However, in a small prospective, randomized trial[5] it was shown that implant survival and the rate of post-treatment complications were comparable between patients who had received hyperbaric oxygen treatment and those who had not, questioning its need.

Instead of focusing on implant survival and numbers of patients benefitting from implant-retained mandibular overdentures, this paper would gain considerably in strength if the authors analyzed on which indication it was decided to place implants during ablative surgery or not, as well as which subgroup of patients would benefit most from, and would be willing to be subjected to, delayed implant therapy. On the basis of such analyses, including data from other relevant studies, the authors could have proposed an algorithm for determining which patients should be treated during ablative surgery or should have delayed implant placement. Taking the data from their study and our studies [1-6] into account, we would propose the following algorithm (Fig. 1): only patients without the

need or possibility for primary ablative tumour surgery, patients for whom no prosthetic problems are expected, and patients for whom implant placement during surgery is not possible should not receive primary implants. In these patients, delayed implant placement might be considered when indicated and possible. Thus, more patients will benefit from implant-retained overdentures at an earlier stage after oncological treatment, allowing them to improve their oral function as soon as possible. It would be a great asset to the literature if the authors could add to the proposed algorithm on the basis of the data they gathered for their study.

Fig. 1. Decision-making process for mandibular implant placement during ablative surgery



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